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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/612,852	07/10/2000	Victor N. Krasnykh	D6070CIP	9473

7590

06/19/2002

Dr Benjamin Adler
McGregor & Adler LLP
8011 Candle Lane
Houston, TX 77071

EXAMINER

SORBELLO, ELEANOR

ART UNIT PAPER NUMBER

1632

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/612,852

Applicant(s)

KRASNYKH ET AL.

Examiner

Eleanor Sorbello

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

Response to amendment

1. Applicant's amendment filed 4/2/02, paper number 5 has been entered. Claim 7 has been canceled. **Claims 1-6, 8-15 are pending.** Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.
2. Applicant's arguments are addressed below on a per section basis. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Double Patenting

3. Claims 1, 2, 5, 6, 8, 12 remain rejected under judicially created doctrine of obvious-type double patenting over claims 1-4 of U.S. Patent. 6,210,946.

It is noted that applicants will submit a Terminal Disclaimer when allowable subject matter is obtained.

Claim Rejections - 35 USC § 112

4. Claims 1-6, 8-15, remain rejected under 35 USC § 112, first paragraph for reasons of record. Applicant's arguments have been fully considered but they are not persuasive.

Applicants have now canceled claim 7, directed specifically at adenoviral vectors with the fiber replacement protein T4 fibrin protein. However, the claims still broadly read on an adenovirus comprising a replacement fiber protein comprising a novel tropism and maintaining trimerization.

The rejection of claims 1-6, 8-12 are discussed herein. Applicants argue that the overall structural and functional similarity of the fiber protein in adenoviruses have been exploited successfully by other investigators who have replaced all or part of the fiber protein of one adenovirus serotype with that derived from another adenovirus serotype. Applicants further argue that the current application is different because they disclose an adenovirus comprising a fiber replacement protein comprising (a) an external trimerization motif to replace the (knobless) fiber and (b) a novel targeting ligand. They argue that the recombinant virion of the instant invention has a novel tropism due to the splitting of the functions of trimerization and ligand binding (normally performed by the knob domain) between two different protein moieties. However, examiner argues that the mechanism of obtaining the novel tropism was not relevant in this case because applicants claim a product made up of specific elements, but examiner argues the breadth claimed. Applicants argue that they replaced the shaft of the fiber with the α -helical portion of the T4 fibrin protein which is a very different rod-like protein composed of different structural units, to the native fiber protein, and thus demonstrated a novel tropism. Therefore, examiner argues that as stated in the scope of enablement in previous office action, applicants are enabled for an adenovirus comprising only one fiber replacement protein, the T4 fibrin protein. However,

Art Unit: 1632

applicants have now canceled claim 7, drawn specifically to that protein. Applicants however, broadly claim that one of skill would be able to make any fiber replacement protein without undue experimentation. Applicants claim that other trimeric proteins can be used in the replacement protein and that the specification discloses the aforesaid. However, in unpredictable fields such as this, the onus is on the applicants to provide support for that which is claimed via experimentation and show that the adenovirus comprising these replacement proteins will actually possess a novel tropism which it is expected to have and hereby claimed. Applicants argue that they have shown that by replacing the fiber protein with (T4 fibrin) which is a rod-like trimeric protein composed of different structural units and that one of skill should be able to construct an artificial protein having a coiled-coil secondary structure, as a replacement protein. However, examiner argues that by merely replacing the fiber protein with one of coiled-coil secondary structure, it will require undue experimentation to test if the replacement protein resulted in a novel tropism and one that is able to trimerize. However, this is not the case and without actually demonstrating such, it is not clear if what is expected will actually occur. Broadly extrapolating from one example of a specified fiber replacement protein to any artificial fiber protein that will provide trimerization, and other limitations encompassed by the claims will require undue experimentation on the part of the artisan as explained in the first office action due to the nature of the invention, state of the art as evidenced by Wickham (col. 2, lines 10-15), and lack of guidance in the specification.

The rejection of claims 13-15 are discussed herein. Applicants argue with examiners rejection of claims 13-15, based on the fact that gene therapy is not enabled and is unpredictable. Applicants argue that the claims do not encompass gene therapy but that the focus of their invention is making and using recombinant adenoviruses that do not bind to the cognate cell surface receptor, but instead has a novel tropism. However, examiner argues that the claims (13-15) are directed to an adenovirus with a novel tropism that comprises a gene with the intended use of therapy, specifically for killing tumor cells. Applicant argues that it is routine in the art to replace marker genes in vector constructs with other genes of interest and that it would not involve undue experimentation to insert a gene expressing a therapeutic protein. However, examiner argues that the vector construct of the instant invention is not enabled for the reasons given in the preceding paragraph. Therefore, the inclusion of known genes in a non-enabled construct would not be routine in the art. Examiner agrees that HSV-TK and gangliclovir are used in methods for killing tumor cells. However, as stated in the first office action, applicants failed to teach targeting ligands specific for tumor cells, or ligands that would infect of tumor cells, using the vector of the instant invention. Neither did the specification teach how the vectors are to be administered, compositions in which they are to be administered, delivery methods or more importantly that a therapeutic level of expression could be achieved for any disease, specifically cancer.

Therefore, the claims remain rejected for reasons stated above.

Conclusion

5. Claims 1-6, 8-15 remain rejected.
6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 308-0009.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or


Application/Control Number: 09/612,852

Page 7

Art Unit: 1632

proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Eleanor Sorbello


DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600